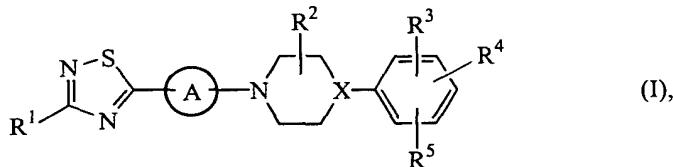


Claims

1. A compound of formula (I),

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the *N*-oxide forms, the pharmaceutically acceptable acid addition salts and stereochemically isomeric forms thereof, wherein

X is CH or N;

10 R<sup>1</sup> is hydrogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylthio, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, Ar<sup>1</sup>, Ar<sup>1</sup>NH-, C<sub>3-6</sub>cycloalkyl, hydroxymethyl or benzyloxymethyl;

R<sup>2</sup> is hydrogen, C<sub>1-6</sub>alkyl, amino, aminocarbonyl, mono- or di(C<sub>1-6</sub>alkyl)amino, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkylcarbonylamino, hydroxy or C<sub>1-6</sub>alkyloxy;

15 R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, trifluoromethyl, nitro, amino, cyano, azido, C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylthio, C<sub>1-6</sub>alkyloxycarbonyl or Het<sup>1</sup>;

—(A)— is Ar<sup>2</sup>, Ar<sup>2</sup>CH<sub>2</sub>- or Het<sup>2</sup>;

20 Ar<sup>1</sup> is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino or nitro;

Ar<sup>2</sup> is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino or nitro;

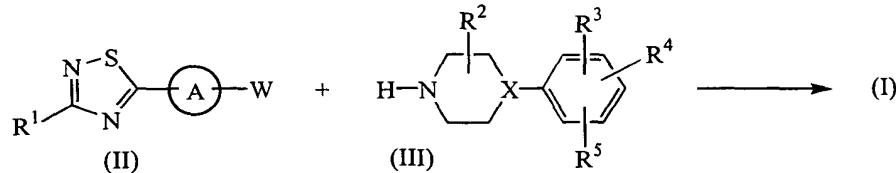
Het<sup>1</sup> is a monocyclic heterocycle selected from oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl or oxazolinyl; and each monocyclic heterocycle may optionally be substituted on a carbon atom with C<sub>1-4</sub>alkyl; and

25 Het<sup>2</sup> is a monocyclic heterocycle selected from furanyl, thifuranyl, oxadiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl; and each monocyclic heterocycle may optionally be substituted on a carbon atom with 1 or 2 substituents each independently selected from halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, nitro or trifluoromethyl.

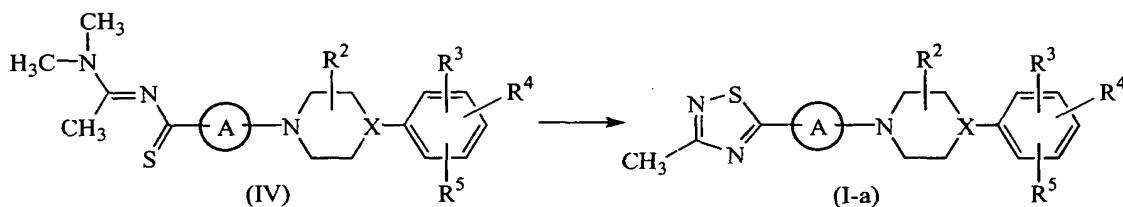
2. A compound according to claim 1 wherein X is N; R<sup>1</sup> is hydrogen, C<sub>1-6</sub>alkyl, amino or di(C<sub>1-6</sub>alkyl)amino; R<sup>2</sup> is hydrogen; R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, trifluoromethyl, nitro or C<sub>1-6</sub>alkyloxycarbonyl.  
5
3. A compound according to any of claims 1 or 2 wherein X is N; R<sup>1</sup> is hydrogen, C<sub>1-4</sub>alkyl or di(C<sub>1-4</sub>alkyl)amino; R<sup>2</sup> is hydrogen; R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy or trifluoromethyl; and the bivalent radical —— is Ar<sup>2</sup>, Ar<sup>2</sup>CH<sub>2</sub>- or Het<sup>2</sup>  
10 wherein Ar<sup>2</sup> is phenyl and Het<sup>2</sup> is thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl..
4. A compound according to any of claims 1 to 3 wherein X is N, R<sup>1</sup> is methyl, R<sup>2</sup> is hydrogen, R<sup>3</sup> and R<sup>4</sup> are hydrogen and R<sup>5</sup> is trifluoromethyl  
15
5. A compound according to claim 1 wherein the compound is 1-[4-(3-methyl-1,2,4-thiadiazol-5-yl)phenyl]-4-[3-(trifluoromethyl)phenyl]-piperazine; or 1-[5-(3-methyl-1,2,4-thiadiazol-5-yl)-2-pyridinyl]-4-[3-(trifluoromethyl)phenyl]-piperazine; a stereoisomeric form or a pharmaceutically acceptable acid addition salt thereof.  
20
6. A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 to 5.  
25
7. A process of preparing a pharmaceutical composition as claimed in claim 6 wherein the pharmaceutically acceptable carriers and a compound as claimed in claim 1 to 5 are intimately mixed.  
30
8. A compound as claimed in any one of claims 1 to 5 for use as a medicine.
9. Use of a compound as claimed in any one of claims 1 to 5 for the manufacture of a medicament for the treatment of angiogenesis dependent disorders.  
35
10. A process of preparing a compound as claimed in claim 1, wherein

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a) an intermediate of formula (II) is reacted with an intermediate of formula (III) in a reaction-inert solvent and, optionally in the presence of a suitable base;



b) an intermediate of formula (IV) is treated with hydroxylamino-O-sulfonic acid in a reaction-inert solvent, in the presence of a suitable base, thereby yielding compounds of formula (I-a), defined as compounds of formula (I) wherein R<sup>1</sup> is methyl;



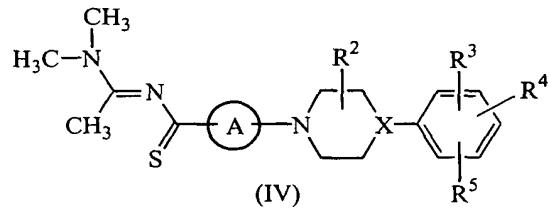
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wherein in the above reaction schemes the radicals X, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and  $\text{---} \textcircled{A} \text{---}$  are as defined in claim 1, and W is an appropriate leaving group;

c) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

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11. A compound of formula (IV),

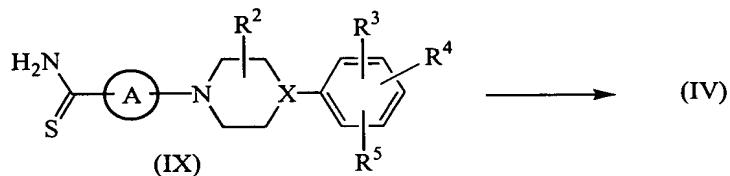


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an acid addition salt, a *N*-oxide form or a stereochemically isomeric form thereof, wherein X, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and the bivalent radical —  — are as defined in claim 1.

5 12. A process of preparing a compound of formula (IV) as claimed in claim 10,  
wherein  
a) an intermediate of formula (IX) is treated with *N,N*-dimethylacetamide dimethyl  
acetal in a reaction-inert solvent, thereby yielding a compound of formula (IV);

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b) or, compounds of formula (IV) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (IV) is converted into an acid addition salt, or conversely, an acid addition salt of a compound of formula (IV) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.